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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/606,137	06/28/2000	Michael E. Moseley	500.003US1	5608

7590

03/25/2003

Mark A Litman
Mark A Litman & Associates PA
York Business Center Ste 205
3209 W 76th Street
Edina, MN 55402

EXAMINER

LIN, JEYUHU

ART UNIT

PAPER NUMBER

3737

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/606,137

Applicant(s)

MOSELEY ET AL.

Examiner

Jeoyuh Lin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 December 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-43 and 47-52 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-43 and 47-52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Entry of Amendment

1. Applicant's amendment, filed on December 31, 2002, as paper No. 11, is acknowledged. Claims 1-43 and 47-52 are currently pending.

Claim Objections

2. Claims 32 and 49 are objected to because of the following informalities:

-In claim 32, line 10, the word, "implantof" should be spelled, "implant of".

-There are two claim 49s.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

-Claims 1-43, and 47-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an MRI method, does not reasonably provide enablement for a sensing method that detect the viability of implanted stem cells, progenitor cells, or differentiated cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claimed invention is drawn to methods of indicating viability of "implanted cells, progenitor cells, or differentiated cells". However, there is very limited guidance within the specification as to how this is to be accomplished. The claimed methods

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(referring to the broadest claim) require a "sensing" function of cells within a region of a patient. The specification at page 5, beginning on line 18 indicates that "no disclosures are known that provide a method or device for...non-invasively monitoring the physiologic and metabolic status of a cell implant". Continuing on page 5, at line 24, the specification states that the "present invention provides an MR imaging method...". However, at least the broad claim is drawn to any sensing method and is not limited to MRI methods. Therefore, a breadth issue exists regarding the scope of the disclosure versus the "sensing" function set forth in the claimed invention.

In discussing the MRI methods, art-recognized metabolic changes are to be assayed. These include such things as observing GABA, PCr, creatine, choline, and lactate metabolites (page 6, lines 4 and 5). The specification also discusses labeling strategies with such markers as C13, F19, N14, S33, H2, Mg, Fe, and other MR-sensitive nuclei (Pg 6 and 7). It is acknowledged that these types of markings are known in the art. However, the claimed invention requires an analysis of very specific type of cells (i.e. stem cells, progenitor cells, and differentiated cells and such general labels while viewable via MRI are not cell type specific). Once a cell is introduced within a host, unless there is some discernable factor which can be specifically detected, (whether it be metabolic, anatomic, or labelable), the cell is inseparable from surrounding cells. In the instant case, the cells are of specific types and the specification fails (with one exception) to provide any guidance as to how one would detect them.

On page 29, beginning at line 3, the specification indicates that, "the ability to monitor correct cell placement non-invasively with MR imaging is currently not available." The specification then goes on to state that in a preferred embodiment, MR is used to detect cells that have been labeled with a detectable marker (in this case Green Fluorescent protein, GFP). This is the only guidance present in the as filed specification as to how to detect a particular cell that has been implanted into a host.

Given the paucity of guidance regarding any inherent property (metabolic, anatomic, or labelable) of stem cells, progenitor cells, it would seem that the claimed methods should be limited to the detection of cells that have been specifically labeled or marked prior to implantation. The concept of the disclosed invention is that one can then find such cells using non-invasive MRI methods, which could be enabling. Thus, there is at least a prima facie case that the claimed methods should be limited to MRI methods and the use of ex-vivo-labeled cells where the label is suitable for MRI methods. Note however, that cells used for implantation have been marked in the prior art for some time using things such as metabolic and other markers (including drug resistance markers and GFP (as disclosed in provisional US patent 60/082,941). Therefore, a prior art issue may be raised based upon whether or not the prior art would have expected to be able to detect, at least, GFP-marked cells.

In summary, the specification fails to provide a general guidance as to how to detect specific cells within a host that do not have MRI detectable properties, and it also fails to teach what such properties would be for any stem cell, any and all "progenitor cells", and any and all "differentiated" cells.

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4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

-Claims 50-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 50 recites the limitation "transplanted cells" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Response to Arguments

5. Applicant's arguments with respect to claims 1-43 and 47-52 have been considered but are not persuasive.

Applicants claim that they have disclosed all of the various imaging or non-destructive testing method to analyze for cell viability. While applicants do describe various ways to analyze cell viability in the broad sense, the applicants fail to describe any specific method for implementing the broad method and analyze a particular cell type, such as a stem cell, or a progenitor cell, each of which would require a specific type of analysis and method step. Also, the description substantially states an MR based detection of cell viability. While it includes the possibility of other types of detection, such as optical, ultrasound, electrical, and fluorescent detection of cell viability, once again no specific method was described to pinpoint and study the viability of one type of cell, in such a way that would enable one having ordinary skill in the art to read the disclosure, discern the specific steps, and reduce the method to practice. Furthermore, the applicants themselves admitted in page 5 of the specification that, "no

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disclosures are known that provide a method or device for...non-invasively monitoring the physiologic and metabolic status of a cell implant." Since there is no admitted prior art on the subject matter, and the current application fails to specifically disclose a method complete with necessary steps to monitor the physiologic and metabolic status of a cell implant that is apart from the rest of the cells in the tissue, the examiner maintains his rejection.

Conclusion

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

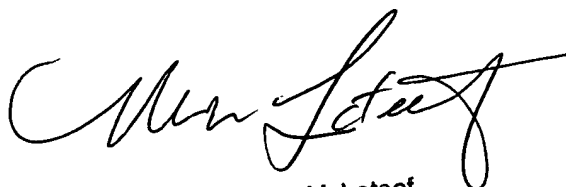
7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeoyuh Lin whose telephone number is (703) 306-5990. The examiner can normally be reached on m-f, 8:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marvin Lateef can be reached on (703) 308-3256. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0758 for regular communications and (703) 308-0758 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0858.

JYL

JYL
March 18, 2003



Marvin M. Lateef
Supervisory Patent Examiner
Group 3700